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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,568	12/07/2001	Chandra S. Ramanathan	D0077 NP	7187
23914	7590	08/13/2004	EXAMINER ZARA, JANE J	
STEPHEN B. DAVIS BRISTOL-MYERS SQUIBB COMPANY PATENT DEPARTMENT P O BOX 4000 PRINCETON, NJ 08543-4000			ART UNIT 1635	PAPER NUMBER
DATE MAILED: 08/13/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/010,568	RAMANATHAN ET AL.
	Examiner	Art Unit
	Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
 THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 May 2004.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 43-60 is/are pending in the application.
 4a) Of the above claim(s) 59 and 60 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 43-58 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 07 December 2001 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>2/19/03, 2/19/03, 2/20/03</u> | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input checked="" type="checkbox"/> Other: <u>Sequence non-compliance</u> . |

DETAILED ACTION

This Office action is in response to the communications filed 12-17-03 and 5-20-04.

Claims 43-60 are pending in the instant application.

Election/Restrictions

Claims 59 and 60, and SEQ ID Nos: 52, 53, 54 and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the replies filed on 12-17-03 and 5-20-04.

Applicant's election without traverse of Group I, claims 43-58, and SEQ ID NO: 51 in the replies filed on 12-17-03 and 5-20-04 is acknowledged.

Claim 1 link(s) inventions SEQ ID Nos: 51, 52, 53, 54 and 55. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction

requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Information Disclosure Statement

Document numbers WO 02/057441 (filed 2-20-03) and WO 02/16548 (filed 12-17-03) were not translated and are in Japanese. The abstracts for these documents were the only portions provided in English, and so were the only portions of the documents considered by the examiner. Document DE 10046970A1 (filed 2-20-03) is in German and has not been translated and has not been considered by the examiner.

Specification Objection and Claim Rejections - 35 USC § 112

This application does not comply with the rules for the deposit of biological material as set forth below in the Suggestion for Deposit of Biological Material. For ATCC deposits, please be sure to use the current address in Virginia, rather than the former address in Maryland.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to and claims 43-58 are rejected under 35 USC § 112, first paragraph as failing to provide an enabling disclosure for the claimed invention.

The application discloses Patent Deposit No. PTA-2966 (e.g. page 8 of the instant specification) that is encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809.

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a declaration or applicant's representative must provide a statement. The content of such a declaration or statement is suggested by the enclosed attachment. Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to

practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.
2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).
3. States that the deposited material has been accorded a specific (recited) accession number.
4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).
5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).
6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).
7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made

are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

Claim Objections

Claim 46 is objected to because claim 46 (lines 3-7) recites "an compound," which is grammatically incorrect (replacing "an" with -a—would be remedial).

Claim 46 is objected to as being drawn to non-elected inventions, SEQ ID Nos: 52, 53, 54 and 55. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 55 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 55, line 2 recites “a heterologous polypeptide” and it is unclear what is meant by the term “heterologous,” because it cannot be determined what the polypeptide is heterologous to (e.g. Is it heterologous to the antisense oligonucleotide of claim 45, or heterologous to the target polypeptide of claim 43, or both?). Appropriate clarification is requested.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43-45, 47-58 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Colote et al.

Colote et al (USPN 5,856,461) teach an antisense compound between 10 and 50 nucleobases in length (col. 1, line 65-col. 2, line 25; col. 3, lines 1-8) that specifically hybridizes to SEQ ID NO: 1 (See SEQ ID NO: 3 of Colote, and the accompanying sequence alignment data), which compound is optionally comprised of DNA, RNA or a combination of DNA and RNA, is optionally single stranded or double stranded (col. 2, lines 33-59), is within a recombinant vector and expressed by an appropriate host cell (col. 1, line 54-col. 2, line 49), and which antisense optionally comprises at least one modified internucleotide linkage, modified sugar moiety or base (nucleotide) and optionally further comprises a heterologous polypeptide (col. 3, lines 16-47; claims 2 and 3). Based on the breadth of "specifically hybridize," this oligonucleotide would meet the structural limitations of the claimed oligonucleotide, because the oligonucleotide is within the size range of 10 to 50 nucleobases and is fully complementary to the nucleic acid of SEQ ID NO: 1 and would hybridize to such. Accordingly, the oligonucleotide disclosed by Colote et al would specifically hybridize as claimed. The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression as claimed falls to applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 USC 102, on 'prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof

is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing In re Fitzgerald 205 USPQ 594, 596 (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the oligonucleotide disclosed by Colote et al would or would not have the additional "functional limitation" of "inhibiting expression" of SEQ ID NO: 1.

Therefore, absent evidence to the contrary, claims 43-45, 47-58 are anticipated by or, in the alternative, obvious over Colote et al.

Claims 43-45, 47-53, 56-58 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Pavco et al.

Pavco et al (WO 97/15662) teach an antisense compound between 10 and 50 nucleobases in length that specifically hybridizes to SEQ ID NO: 1, which compound is optionally comprised of DNA, RNA or a combination of DNA and RNA, (see page 5, line 23-page 7, line 10; page 9 lines 14-35; page 12 lines 3-15), is optionally single stranded or double stranded (page 6, line 22-page 7, line 7; page 19, line 5-page 20, line 29; page 24, lines 5-37), is within a recombinant vector and expressed by an appropriate host cell (page 10, line 34-page 11, line 21), and which antisense optionally comprises at least one modified internucleotide linkage and one modified sugar moiety (page 17, lines 23-30; page 22, lines 11-20) (See also Accession # AAX74847 of Pavco et al and the accompanying sequence alignment data: It is noted that the specification as filed

states that the sequence of an antisense need not be 100% complementary to that of its target nucleic acid to be one that "specifically hybridizes," as claimed in the instant invention (e.g. see claim 43, line 1 and page 21 of the instant specification). Based on the breadth of "specifically hybridize," this oligonucleotide would meet the structural limitations of the claimed oligonucleotide, because the oligonucleotide is within the size range of 10 to 50 nucleobases and is 88% complementary to the nucleic acid of SEQ ID NO: 1 and would hybridize to such. Accordingly, the oligonucleotide disclosed by Pavco et al would specifically hybridize as claimed. The burden of establishing whether the prior art oligonucleotide has the further function of inhibiting gene expression as claimed falls to applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 USC 102, on 'prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced b the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594, 596 (CCPA 1980), quoting *In re Best* 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the

oligonucleotide disclosed by Pavco et al would or would not have the additional "functional limitation" of "inhibiting expression" of SEQ ID NO: 1.

Therefore, absent evidence to the contrary, claims 43-45, 47-53, 56-58 are anticipated by or, in the alternative, obvious over Pavco et al.

Allowable Subject Matter

SEQ ID NO: 51 in claim 46 is free of the prior art searched and of record.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **The sequences in figures 2b and 2c must be accompanied by appropriate and corresponding SEQ ID Nos.** See the accompanying Notice to Comply.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ
7-28-04

J Zara
TC 1600

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- 7. Other: Please provide accompanying SEQ ID Nos. for the sequences disclosed in figures 2a and 2b.

Applicant Must Provide:

- An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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